8/12/04 CM

Amendments to the Specification:

Please replace paragraph [0001] with the following amended paragraph:

[0001] This application claims the benefit of U.S. Provisional Application Nos. 60/126,839, filed March 30, 1999; 60/140,073, filed June 21, 1999; 60/147,071, filed August 4, 1999; 60/160,524, filed October 20, 1999; 60/160,669, filed October 21, 1999; 60/172,744, filed December 20, 1999; and No. ~~_____~~; 60/178,184, filed January 26, 2000.

Application Serial No. 09/936,024 Attorney Docket No. X-12799, herein incorporated by reference.

In vitro studies suggest that FLINT metabolite binds FasL with an apparent lower affinity than FLINT. Therefore, the pharmaceutical utility of FLINT could be enhanced by an analog that is resistant to proteolysis at or near the 218 position. The invention disclosed herein provides such analogs.

In one embodiment, the invention relates to a FLINT analog that is resistant to proteolysis between positions 218 and 219 of SEQ ID NO:1, and/or between positions 247 and 248 of SEQ ID NO:3 *in vivo* and/or *in vitro*.

In another embodiment, the invention relates to a FLINT analog that is substantially resistant to proteolysis between positions 218 and 219 of SEQ ID NO:1, and/or between positions 247 and 248 of SEQ ID NO:3 *in vivo* and/or *in vitro*.

In another embodiment, the invention relates to a FLINT analog that is resistant to proteolysis by a trypsin-like protease between positions 218 and 219 of SEQ ID NO:1, and/or between positions 247 and 248 of SEQ ID NO:3 *in vivo* and/or *in vitro*.

In another embodiment, the invention relates to a FLINT analog that is resistant to proteolysis by a serine protease, for example, trypsin, thrombin, or chymotrypsin between positions 218 and 219 of SEQ ID NO:1, and/or between positions 247 and 248 of SEQ ID NO:3, *in vivo* and/or *in vitro*.

In another embodiment, the invention relates to a FLINT analog that is resistant to proteolysis by a trypsin-like protease between positions 218 and 219 of SEQ ID NO:1, and/or between positions 247 and 248 of SEQ ID NO:3, said

SEQ ID NO:3 - Native human FLINT.

SEQ ID NO:4 - Human FLINT leader sequence.

SEQ ID NO:5 - Oligonucleotide primer A, CF107

SEQ ID NO:6 - Oligonucleotide primer B, CF111

SEQ ID NO:7 - Oligonucleotide primer C, CF112

SEQ ID NO:8 - Oligonucleotide primer D, CF110

SEQ ID NO:9 - Nucleic acid/cDNA encoding native human FLINT

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1. Time course thrombin cleavage of native FLINT and R218Q analog.

Figure 2. FLINT analog R218Q inhibits FasL-induced apoptosis in Jurkat cells. FLINT samples purified from AV12 cells.

Figure 3. FLINT analog R218Q purified from 293 EBNA cells inhibits FasL induced apoptosis in Jurkat cells.

Figure 4. FLINT analog RDDSR inhibits FasL-induced apoptosis in Jurkat cells.

Figure 5. RP-HPLC profile of radioactivity after an *in vitro* incubation of ^{125}I-FLINT and ^{125}I-FLINT(R218Q) with ICR mouse blood. Test articles were incubated for 1 h at 37° C. Serum was prepared and fractionated by RP-HPLC. Data is expressed as the percentage of radioactivity per fraction applied to the column.

Figure 6. RP-HPLC profile of FLINT immunoreactivity in plasma 15 min. after an intravenous administration of FLINT, or FLINT (R218Q), to ICR mice. Fractions were collected and analyzed by ELISA. Data are representative of findings from each individual animal.

Figure 7. FLINT and FLINT analog dose response in mouse acute liver failure (ALF) model.

The term "analog" or "FLINT analog" means a variant FLINT, or fragment thereof, resistant to proteolysis between